

The Applicants respectfully traverse the rejection. The Examiner has engaged in impermissible, hindsight reconstruction to pick and choose among the prior art in order to try to fashion a rejection of the claimed invention.

The Examiner asserts that a person of ordinary skill in the art would have been motivated to culture human HSCs by the methods taught in the relevant cited patents and articles, to transfect them with genes using retroviral vectors as taught by the relevant cited articles, and to increase transduction efficiency through the use of fibronectin, also as taught by the relevant cited articles. However, the Examiner is required to show how and why the Applicants would have been motivated to combine the references in the manner combined by the Examiner. The Examiner has not done so. She has simply made unsupported statements regarding the asserted motivation of a person of ordinary skill in the art to undertake the components of the claimed invention.

On page 6 of the Office Action, the Examiner asserts that a person of ordinary skill in the art: (1) would have had an expectation of success to culture HSCs in the various factors specified in the claims; (2) would have had an expectation of success to modify such HSCs in culture using retrovirally-mediated gene transfer; and (3) would have had an expectation of success to increase transformation efficiency of the retroviruses through the use of fibronectin. However, the question with respect to patentability of the claimed invention is **not** whether a person of ordinary skill in the art would have had a reasonable expectation of success with respect to individual components of the claimed invention, but whether that person would have had a reasonable expectation of success with regard to the combination of all of the components of the invention, i.e., whether the **invention as a whole** was obvious. The Examiner has not shown that the **invention as a whole** was obvious. In fact, the Applicants remind Examiner of her statements of record in her Office Action of May 12, 1999, where, at the bottom of page 5, she stated that "There is a high level of unpredictability in the transgenic stem cell art for expression of transgenes in cultured stem cells." Given this unpredictability, a person of ordinary skill in the art would not have had a reasonable expectation of success with respect to the claimed **invention as a whole**.

Furthermore, the Examiner has not shown how the cited references teach the concentration ranges recited in the claims. The Examiner has cited references where certain factors in the claims were used at certain concentrations, but she has made no showing of how the references teach the recited **ranges** of concentrations.

Finally, the Applicants note that claims 35, 44, and 51 are directed to CD34⁺ Thy-1⁺ Lin⁻ HSCs. The Examiner has not shown how the cited references teach the genetic modification of these particular HSCs in the presence of the factors and at the concentration ranges recited in the claims.

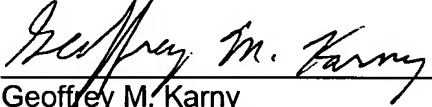
For the above reasons, the rejection is in error and should be withdrawn.

The Examiner noted the use of a trademark in the application. The Applicants believe that they have met all the legal requirements with respect to the use of the mark.

The Applicants respectfully submit that claims 18-20, 23-27, 31-35, 37-44, and 46-51 are in condition for allowance.

Respectfully submitted,

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